A BRIEF INTRODUCTION TO THE PHYTOSOME

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ABSTRACT:

In contemporary times, medicinal plants and their constituent phytochemicals have become significant therapeutic alternatives for various conditions. Nevertheless, their clinical utility may be restricted by inadequate bioavailability and specificity. Consequently, bioavailability represents a critical hurdle in enhancing the biological efficacy of phytochemical transport from dietary sources. Various methodologies have been suggested to develop efficient carrier mechanisms that improve phytochemical bioavailability. Within this context, nano-vesicles have emerged as encouraging options for delivering insoluble phytochemical compounds.

Across the cosmos, botanical remedies have been utilized comprehensively since ancient epochs and have garnered recognition from healthcare professionals and laypeople alike owing to their enhanced therapeutic efficacy and reduced adverse reactions relative to contemporary pharmaceuticals. The term "Some" pertains to cellular structures, whereas "Phyto" denotes botanical origins. This innovation is frequently designated as "herbosomes," a pioneering, proprietary methodology wherein phospholipids enhance absorption and bioavailability substantially through the conversion of hydrophilic phytoconstituents or standardized botanical extracts into lipid-compatible molecular complexes.

KEYWORDS: Bioavailability,Drug Deliver, Delivery system,Phytosome,Phytophosolipid

INTRODUCTION:

1.1 Importance of Phytosomes: Phytosomes represent a vesicular drug delivery system characterized by phytoconstituents and lipid components on both sides. When administered orally or topically, herbal extracts demonstrate enhanced absorption. The term phyto and related terminology describe cell-like structures. Phytosomes possess the capability to traverse the lipophilic pathway of enterohepatic cell membranes. Among the utilized phospholipids—phosphatidylcholine (PC), phosphatidylserine, phosphatidylethanolamine, and phosphatidylinositol—PC is predominantly employed due to its therapeutic efficacy against hepatic conditions including hepatitis, alcoholism, alcoholic steatosis, and drug-induced hepatic injury. Ginkgo biloba phytosome diminished the levels of TNF-induced PDGF, CXCL10, and RANTES, as well as the baseline PDGF release. Research indicates that lipoic acid exhibited more extensive and potent inhibitory effects on cytokine and chemokine release compared to Ginkgo biloba phytosome. The study demonstrated that while Ginkgo biloba appeared to have specific effects, lipoic acid significantly suppressed TNF-induced NF-B and p38/MAPK activation.[12]

1.2 The Transdermal drug delivery system (TDDS) represents an attractive alternative to oral drug administration and potentially offers a substitute for hypodermic injection. Historically, humans have utilized herbal extracts and chemicals topically for therapeutic aims over millennia, and the modern era has witnessed the development of numerous topical formulations designed to address localized conditions . Transdermal administration presents multiple advantages compared to oral routes. It is particularly beneficial when significant first-pass hepatic effects might result in premature drug metabolism. Furthermore, transdermal delivery methods demonstrate superiority over hypodermic injections, which are associated with discomfort, generate hazardous medical waste, and present risks of disease transmission through needle reuse, especially in economically disadvantaged regions.[5]

1.3 The majority of plants' biologically active components are polar or water-soluble; however, absorption difficulties limit the utilization of these compounds, consequently reducing their bioavailability. To enhance bioavailability, herbal preparations require appropriate homeostasis between hydrophilic properties (necessary for absorption into gastrointestinal tract fluid) and lipophilic characteristics (essential for crossing lipid biomembrane

2. CHARACTERISTICS OF PHYTOSOME:

2.1 Physicochemical Characteristics: A phytophospholipid complex comprises a natural substance combined with organic phospholipids, typically derived from soy. This complex formation occurs through the reaction of stoichiometric amounts of phospholipids and the substrate in an appropriate solvent. Spectroscopic evidence indicates that the primary interaction between the phospholipids and substrate results from hydrogen bond formation between the phospholipids' polar head (specifically the phosphate and ammonium groups) and the substrate's polar functional groups.[11]

2.2 Biological Characteristics: When administered orally, phytosome enhances the active absorption of constituent substances and increases their systemic bioavailability. These formulations represent an advancement over conventional herbal extracts and demonstrate greater efficacy. The pharmacokinetic profile of phytosome is superior compared to that of standard herbal medicinal preparations.[6]

3. ADVANTAGES OF PHYTOSOME:

3.1 Increase of drug/molecules stability thanks to the encapsulation

3.2 Non-toxic, flexible, biocompatible, biodegradable, and nonimmunogenic:

3.3 Increase of efficacy and therapeutic index of drug

3.4 Reduction in toxicity of the encapsulated agents

3.5 Reduction of the exposure of sensitive tissues to toxic drugs

3.6 Site avoidance effect

3.7 Improved pharmacokinetic effect[23]

4. DISADVANTAGES OF PHYTOSOME

4.1. Low solubility
4.2. Short half-life
4.3. Possibillity of phospholipid oxidation and hydrolysis-like reaction

4.4. Leakage and fusion of encapsulated drug/molecules
4.5. High production costs
4.6. Fewer stables

5. GENERAL METHOD OF PREPARATION:

In the phytosome preparation process, specific quantity of phospholipid—soy lecithin—is incorporated with plant extracts in an aprotic solvent. Phosphatidylcholine, the main constituent of soy lecithin, fulfills dual functions. The phosphatidyl segment, being lipid soluble, connects to the choline bound complex, while the choline portion attaches to the hydrophilic primary active ingredients. This interaction generates a more stable and bioavailable lipid complex. An alternative phytosome synthesis method involves reacting phospholipid, either synthetic or natural, with standardized plant extract in a ratio ranging from 0.5 to 2.0, though a 1:1 ratio is generally preferred. The resultant complex can be isolated via lyophilization, spray-drying, or precipitation using a non-solvent (typically an aliphatic hydrocarbon). This reaction may occur in a singular aprotic solvent such as acetone, methylene chloride, or dioxane, or in a natural combination.

Phytosome vesicles were produced utilizing a thin layer rotary evaporator vacuum technique. The phytosomal complex was combined with anhydrous ethanol in a 250 ml round-bottom flask attached to a rotary evaporator. The solvent evaporates at approximately 60°C, forming a thin coating on the flask's interior. Hydration of this film with phosphate buffer (7.4) leads to vesicle suspension formation as the lipid layer separates. The phytosomal suspension underwent probe sonication at 60% amplitude and was refrigerated for 24 hours prior to characterization. The reflux method presents another preparation approach, wherein phospholipid and polyphenolic extract in a 100 mL round-bottom flask are refluxed in DCM for one hour at temperatures not exceeding 40°C. Following evaporation of the clear solution, 15 mL of n-hexane was added. The resulting precipitate was subsequently placed in a desiccator.

The protocol suggests precise weighing of phospholipid and cholesterol into a round-bottom flask, dissolution in 10 mL of chloroform, followed by bath sonication for 10 minutes. Organic solvent removal can be achieved via a rotating evaporator at 40°C under reduced pressure. The thin layer, completely devoid of solvent, is then hydrated with the drug's polyphenolic extract in a rotary evaporator. To dissipate heat, the phospholipid mixture underwent sonication in an ice bath. The finished phytosomes were stored in amber-colored vials

6. METHOD OF PREPARATION OF PHYTOSOME:

6.1. Solvent evaporation method: A circular bottom flask (100 mL) containing the requisite quantity of plant material and phospholipids with 20 mL of acetone undergoes reflux for two hours at 50–60°C. Following condensation to 5–10 mL, the mixture is filtered to separate the precipitate. The phytosome complex precipitate is subsequently dried and preserved at ambient temperature in an amber-colored glass vessel.[13]

6.2. Rotary evaporation technique
: The appropriate quantities of plant material and phospholipid are dissolved in 30 mL of tetrahydrofuran within a rotating circular bottom flask. The solution is stirred for three hours at temperatures not exceeding 40°C. After collecting a thin film of the sample, n-hexane is introduced, and the mixture undergoes continuous agitation via magnetic stirrer. The resulting precipitate is extracted and allowed to cool to room temperature in an amber-colored glass container.[14]

6.3. Ether-injection technique: This methodology involves dissolving the drug lipid complex in an organic solvent. Subsequently, vesicles form through gradual injection of this mixture into a heated aqueous agent. The configuration of amphiphiles is concentration-dependent. At low concentrations, amphiphiles exist as monomers, whereas increased concentrations may induce alternative structures including circular, cylinder, disc, cubic, or hexagonal formations.[15]

6.4. Mechanical Dispersion method: This process facilitates contact between the drug-containing aqueous phase and lipids dissolved in organic solvent. Initially, the phytoconstituents for encapsulation are dissolved in diethyl ether, which is then carefully introduced to an aqueous solution. The subsequent removal of organic solvent under reduced pressure induces the formation of the Phyto phospholipid complex. Supercritical fluids (SCF) encompass the compressed anti-solvent procedure (PCA), supercritical anti-solvent method (SAS), and gas anti-solvent technique (GAS).

7. EVALUATION PARAMETERS OF THE FORMULATIONS

A) Particle size
(B)Homogeneity
(C) Drug loading
(D) Drug Entrapment efficiency
(E)Swelling index
(F)Bulk density
G)Tapped Density

8. CHARACTERISTICS OF PHYTOSOME:

- Visualization: Visualization of phytosomes can beachieved using transmission electron microscopy (TEM) and scanning electron microscopy (SEM). With a 1000x magnification, TEM is used to characterize the size of phytosomal vesicles, and SEM is utilized to assess the particle's size and appearance. The dry sample iapplied to a gold-coated brass stub of the electron microscope.[25]
- Particle size and zeta potential: By employing a computerized inspection system and photon correlation spectroscopy (PCS), dynamic light scattering (DLS) can be used to determine the particle size and zeta potential.[22]
- Transition temperature: To determine the vesicular lipid system's transition temperature, differential scanning calorimetry is performed. The drug-phospholipid complex, drug polyphenolic extract, phosphatidylcholine, a physical mixture of the drug extract and phosphatidylcholine, and the drug were all added to an aluminum cell and heated at a rate of 50–250 °C/min from 0 to 400 °C in a nitrogen atmosphere.[21]
- Surface tension measurement: The ring method in a Du Nouy ring tensiometer can be used to assess the drug's surface tension activity in an aqueous solution.[20]
- Entrapment efficiency: The ultracentrifugation method can be used to determine how well a medication is captured by phytosomes. The drug phytosomal complex was centrifuged at 10000 rpm for 90 minutes at 4°C to separate phytosome from the untrapped drug. The concentration of the free drug can be measured by doing ultraviolet spectroscopy.[3]
- Vesicle stability: The stability of vesicles can be estimated by monitoring the size and structure of vesicles over time. DLS measures mean size, while TEM tracks structural changes.[1]
- Drug content: A customized high-performanceliquid chromatographic method or an appropriate spectroscopic method can be used to quantify the amount of medication.[2]
- Evaluation of PhytosomesThe following spectroscopic techniques are employed to confirm the development of a complex or to investigate the reciprocal interaction between the phytoconstituent and the phospholipid

9. APPLICATION OF PHYTOSOME:

- Enhancing Bioavailability:

Phytosomes address the limitations of solubility and stability in certain plant extracts, thereby facilitating enhanced bodily absorption.
This superior absorption capability results in elevated active compound concentrations within the bloodstream, potentially amplifying their therapeutic efficacy.
Phytosomes serve as delivery vehicles for substantial and heterogeneous drugs, including peptides and proteins.[18]

- Therapeutic Applications:

Anti-inflammatory and Anti-cancer:
The improved delivery mechanism of phytosomes for plant extracts with anti-inflammatory and anti-cancer attributes may potentially augment their effectivenes.

- Wound healing

Topical formulations incorporating phytosomes can facilitate wound healing processes through efficient delivery of plant extracts to the injured site.

- Cardiovascular Diseases:

In the management of cardiovascular conditions, phytosomes demonstrate promise by enhancing the delivery of neuroactive phytoconstituents.

- Nervous System Disorders:

Their capacity for enhanced bioavailability and targeted delivery of neuroactive compounds positions phytosomes as a prospective therapeutic strategy for nervous system disorders.[5]

- Liver Protection:

Plant extracts with hepatoprotective properties, such as milk thistle, can be effectively delivered via phytosomes.

- Metabolic Syndrome:

Research has investigated phytosomes for their potential application in managing metabolic syndrome and associated conditions.

- Antioxidant Properties:

Plant extracts with antioxidant characteristics, exemplified by grape seed extract, can be delivered through phytosomes.[9]

10. CONCLUSION:

This paper presents a concise examination of phytosomes as a delivery system. Phytosomes represent cutting-edge formulations that enhance the bioavailability of hydrophilic flavonoids and similar compounds through dermal or gastrointestinal absorption. They exhibit significant distinctions from conventional formulations in various respects. The phytosome manufacturing process is uncomplicated and readily adaptable for industrial production. The analytical methodologies and characterization techniques for this novel formulation type are well-defined. Numerous patents have already been granted for innovative phytosome formulations, methodologies, and applications. Regarding applications for hydrophilic botanical compounds and formulation technology, phytosome technology demonstrates considerable promise for future development.

11. FUTURE ASPECT

The comprehensive literature analysis demonstrates the diversity of phytosome formulations and their distinctive advantages over conventional plant extracts regarding significant therapeutic and health-enhancing properties. Raw, semi-purified, or fractionated plant extracts can undergo standardization before phytosome development for subsequent investigation to identify potential enhancements. Future research might explore combining phytosomes with diverse phytochemicals or incorporating both medications and phytochemicals within a single nano-vesicle to generate stimulatory effects. Phytosomes exhibit similarities to liposomes in terms of dermal penetration capabilities and stability characteristics. Nevertheless, phytosomes are distinguished by the formation of hydrogen bonds with the polar head of the phospholipid.

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